Blood

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The fluid that circulates in the blood vessels of the body. Blood consists of plasma and cells floating within it. The chief components of plasma are proteins (albumin and globulins), anions (mainly chloride and bicarbonate), and cations (mainly sodium, with smaller concentrations of potassium, calcium, and magnesium). The cells are derived from extravascular sites and then enter the circulatory system. They frequently leave the blood vessels to enter the extravascular spaces, where some of them may be transformed into connective tissue cells. The fluid part of the blood is in equilibrium with the tissue fluids of the body. The circulating blood carries nutrients and oxygen to the body cells, and is thus an important means of maintaining the homeostasis of the body. It carries hormones from their sites of origin throughout the body, and is thus the transmitter of the chemical integrators of the body. Blood plasma also circulates immune bodies and contains several of the components essential for the formation of blood clots. Finally, blood transports waste products to excretory organs for elimination from the body. Because of its basic composition (cells surrounded by a matrix), development, and ability to modify into other forms of connective tissues, blood can be regarded as a special form of connective tissue. *See also:* **Connective tissue (/content/connective-tissue/157300)**

Formed Elements

The cells of the blood include the red blood cells and the white blood cells. In all vertebrates, except nearly all mammals, the red blood cells or corpuscles contain a nucleus and cytoplasm rich in hemoglobin. In nearly all mammals the nucleus has been extruded during the developmental stages.

Erythrocytes

In normal adult men, the blood contains about 5,000,000 red blood corpuscles or erythrocytes per cubic millimeter; in normal adult women, about 4,500,000. The erythrocytes in humans are about 8 micrometers in diameter and about 2 micrometers at their thickest and have a biconcave shape. They contain hemoglobin, which imparts to them their color, and possess an envelope, which when viewed with the electron microscope appears highly structured. The hemoglobin is involved in the

transport of oxygen and carbon dioxide and plays a role in maintaining a constant pH in the blood. When circulating in the blood vessels, the red blood cells are not evenly dispersed. In the narrowest vessels, the capillaries, the erythrocytes are often distorted. In certain conditions, they may be densely aggregated. This is known as a sludge. The erythrocytes respond to changes in osmotic pressure of the surrounding fluid by swelling in hypotonic fluids and by shrinking irregularly in hypertonic fluids. Shrunken red blood cells are referred to as crenated cells. The average life of the mature red blood cell is surprisingly long, spanning about 120 days. *See also:* **Hematologic disorders (/content/hematologic-disorders/312800)**; **Hemoglobin (/content/hemoglobin/313800)**

Leukocytes

In humans, the white blood cells in the blood are fewer in number. There are about 5000–9000/mm^3. In general, there are two varieties, agranular and granular. The agranular cells include the small, medium, and large lymphocytes and the monocyte (**Fig. 1**). The small lymphocytes are spherical, about the diameter of erthyrocytes or a little larger, and constitute about 20–25% of the white blood cells. The medium and large lymphocytes are relatively scarce. In all lymphocytes the nucleus occupies nearly the whole volume of the cell, and the cytoplasm which surrounds it forms a thin shell (**Fig. 2***a*). The cytoplasm stains deeply with basic dyes as a result of its high content of ribonucleic acid, which exists in soluble form and in larger aggregates with protein which are known as ribosomes. Ribosomes are about 18 nanometers in diameter, and are grouped in functional clusters called polysomes, which play an important role in protein synthesis. The typical monocyte is commonly as large as a large lymphocyte (12 μm), and constitutes 3–8% of the white blood cells. The nucleus is relatively small, eccentric, and oval or kidney-shaped. The cytoplasm is relatively larger in volume than that in lymphocytes and does not stain as deeply with basic dyes. *See also:* **Ribosomes (/content/ribosomes/589200)**

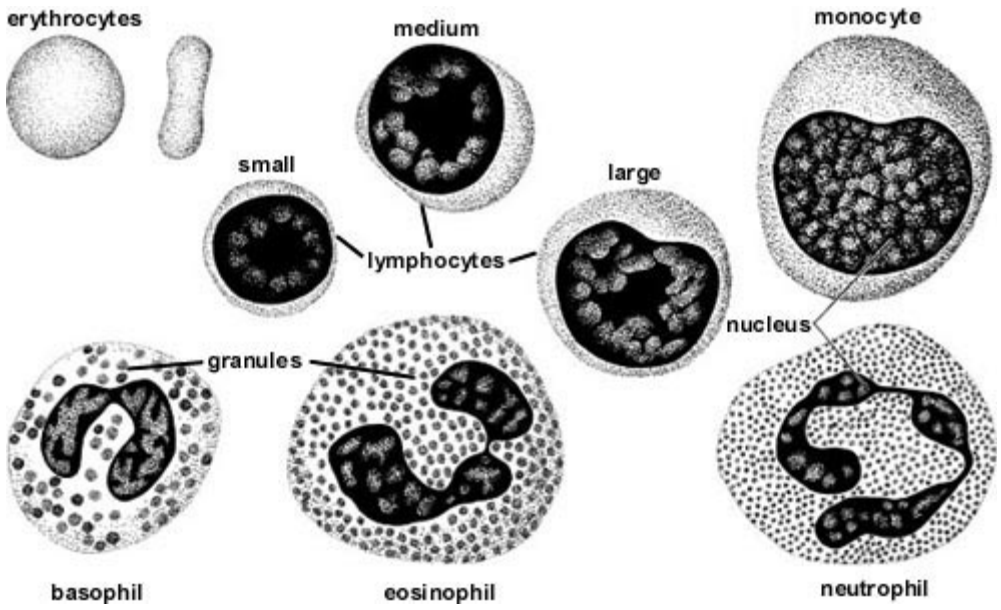

Fig. 1 Diagrams of human blood cells.

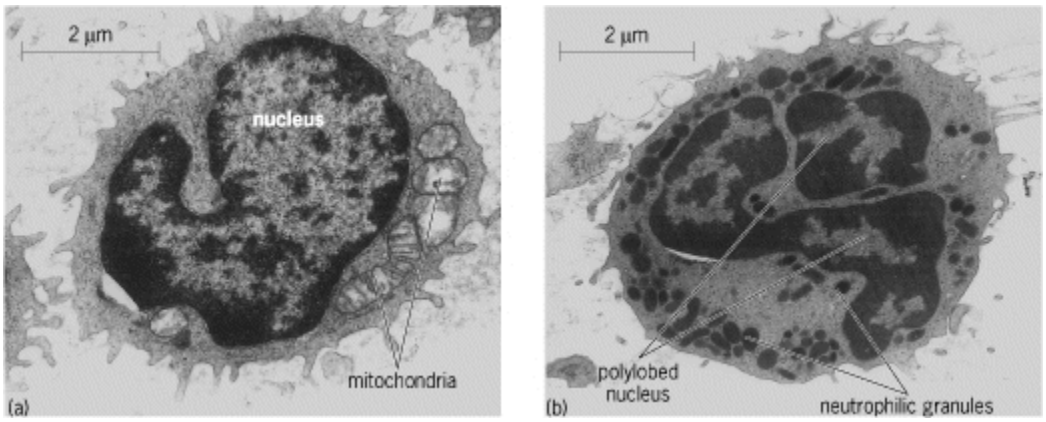

Fig. 2 Low-power electron micrograph of (*a*) lymphocyte and (*b*) neutrophil from the blood of a calf.

The granular white blood cells or granular leukocytes are of three varieties: neutrophil, eosinophil, and basophil. Their structure varies somewhat in different species, and the following applies to those of humans.

The neutrophils make up 65–75% of the leukocytes. They are about as large as monocytes with a highly variable nucleus, consisting of three to five lobes joined together by threads of chromatin (Fig. 2*b*). The cytoplasm contains numerous minute granules which stain with neutral dyes and eosin. In certain conditions, the neutrophils leave the blood vessels and wander into the connective tissue ground substance, where they may then disintegrate, releasing their granules. These granules are rich in certain hydrolytic enzymes, which become active and take part in some phases of the defense mechanisms of the body. The granules are considered to be pure lysosomes which are released from the cell during inflammation and in other conditions, thus liberating many enzymes which are important in combating infections, in cleaning up cell debris, and so on. *See also:* **Lysosome (/content/lysosome/394100)**

The eosinophils (also called acidophils) are about the same size as the neutrophils but are less numerous, constituting about 1% of the leukocytes. The nucleus commonly contains but two lobes joined by a thin thread of chromatin. The granules which fill the cytoplasm are larger than those of the neutrophils and stain with acid dyes.

The basophils are about the same size as the other granular leukocytes. The nucleus may appear elongated or with one or more constrictions. The granules are moderately large, stain with basic dyes, and are water-soluble.

The functions of the leukocytes while they are circulating in the blood are not known. However, when they leave the blood vessels and enter the connective tissue, they constitute an important part of the defense mechanism and of the repair mechanism. Many of the cells are actively phagocytic and engulf debris and bacteria. Lymphocytes are of two major kinds, T cells and B cells. They are involved in the formation of antibodies and in cellular immunity. Lymphocytes develop into plasma cells, which form antibodies even more effectively than lymphocytes. The lymphocytes and plasma cells may act in conjunction with macrophages in promoting phagocytosis. In addition, lymphocytes and monocytes may develop extravascularly into macrophages (which are also phagocytic) and subsequently into fibroblasts. The fibroblasts are important in the formation of new connective tissue in regions of injury. *See also:* **Cellular immunology (/content/cellular-immunology/118100)**; **Phagocytosis (/content/phagocytosis/504200)**

Platelets

The blood platelets are small spindle-shaped or rodlike bodies about 3 µm long and occur in large numbers in circulating blood. In suitably stained specimens they consist of a granular central portion (chromomere) embedded in a homogeneous matrix (hyalomere). They change their shape rapidly on contact with injured vessels or foreign surfaces and take part in clot

formation. During this process numerous fibrils of fibrin radiate from the platelets. The platelets are not to be regarded as cells and are thought to be cytoplasmic bits broken off from their cells of origin in bone marrow, the megakaryocytes.

Hematopoiesis

Some of the blood cells are terminal cells in the sense that they are fully differentiated and have little or no capacity for division. These are the erythrocytes and the granulocytes. The agranular leukocytes may develop extravascularly into other cell types (macrophages, fibroblasts, or plasma cells). All blood cells are formed in the hematopoietic organs (chiefly lymph nodes and spleen for agranular leukocytes, and red bone marrow for erythrocytes and granular lukocytes in the adult). In these organs the blood cells develop from precursor cells which themselves are thought by many to be derived eventually from the least differentiated cells of this strain, the hemocytoblast or primitive mesenchymal cell. *See also:* **Hematopoiesis (/content/hematopoiesis/312900)**

Comparative aspects

Though blood cells occur in all vertebrates, they differ in density, in relative proportions, in morphology to some extent, and in their sites or origin (see **table**).

Range of variation in numbers and relative proportions of blood cells for some vertebrates

Vertebrate	Red blood cells, $\times 10^6$	Blood platelets, $\times 10^4$	Total leukocytes, $\times 10^3$	Relative proportions of leukocytes, %* Lympho-cytes	Mono-cytes	Neutro-phils	Eosino-phils	Baso-phils
Frog	0.2–0.7	0.34–0.39	2.4–25	24–69	2–20	17–72	6–26	1–37
Chicken	3.0–3.8 (3.3)†	1.7–5.0 (3.1)	9.3–32.3 (20)	37–90	0–1	13–49	2–14	1–7
Cat	7–10 (8.5)	15–36.5 (25.8)	8.6–27 (17.8)	10–64	1–3	31–85	1–10	0–2
Dog	5.6–6.8 (6.1)	16.5–37.8	7–11.4 (10)	9–50	1–6	42–77	0–14	0–1
White rat	5.5–10 (8)	43–48	5–25.6 (12.5)	62–75	1–6	18–36	1–4	0
Rabbit	4–6.4 (5.3)	12.6–100 (22)	5.2–12 (8)	20–90	1–4	8–50	1–3	0.5–30
Cow	5–10 (7)	10–80 (50)	4–12	45–75	2–7	15–47	2–20	0–2
Sheep	8–12 (10.8)	26.3–59.8 (40)	6.4–9.8 (8)	38–72	1–3	21–49	0–20	0.5–2
Pig	5.8–8 (6.5)	32.5–71.5 (52)	11–22 (16)	39–62	2–10	28–51	0.5–11	0.2
Horse	6.5–12.5 (9.5)	10–60 (33)	5.5–12.5 (9)	15–70	0.5–10	30–77	0–12	0–3
Elephant	2–4 (2.8)		6.4–14 (10.2)	40–60	0–5	22.50	6–15	0–1
Camel	3.8–12.6 (8.2)		12.9–27.2 (11.7)	27–65	0.1	21–56	0–19	0–1
Lion	6.9–10.9 (9.3)		8.2–19.8 (14.2)	7–37	0–2	54–97	0–6	0
Humans	4.6–6.2 (5.4)	14–44 (25)	5–9 (7)	20–25	3–8	65–75	0–1	0–0.5

*Relative proportion of leukocytes given as a range of total leukocytes per cubic millimeter of blood.
†Number of cells (average in parentheses) given as a range per cubic millimeter of blood.

Although all cell types occur in all vertebrates, there are some morphological variations among the cells. The red blood cells of fish are nucleated, are ovoid or spindle-shaped, and may be larger than in any other vertebrate. They are also large in frogs, where they are somewhat less oval than in birds, and nucleated in both. Notable differences in internal structure of leukocytes are most marked in the size, shape, and staining properties of the granular leukocytes. In the chicken the granules of the neutrophils stain like those of eosinophils and appear rodlike. In the cat the neutrophilic granules are minute, and the eosinophilic granules are rodlike. In the rabbit neutrophilic granules are rather large spheres and stain eosinophilic, while the granules of eosinophils are elongated.

In adult mammals cells of the circulating blood normally arise from bone marrow (red blood cells, granular leukocytes, and platelets), lymph nodules of spleen, lymph nodes, and other lymphoid organs (lymphocytes). But in lower animals (fishes) the connective tissue of the kidney may be important in the origin of all types of blood cells. In other fish the connective tissue of the genitalia may be the site of origin of granulocytes, and the connective tissue of the intestine may be the site of origin of

lymphocytes. The liver of some amphibians may be important for the origin of blood cells.

Isidore Gersh

Plasma

Plasma is the residual fluid of blood left after removal of the cellular elements. Serum is the fluid which is obtained after blood has been allowed to clot and the clot has been removed. Serum and plasma differ only in their content of fibrinogen and several minor components which are in large part removed in the clotting process.

Plasma proteins

The major constituents of plasma and serum are proteins. The total protein concentration of human serum is approximately 7 g/ml, and most other mammals show similar levels. Birds, reptiles, amphibia, and most fishes have lower protein concentrations of approximately 3–5 g/100 ml. By various methods it can be demonstrated that serum protein is a heterogeneous mixture of a large number of constituents. Only a few are present in higher concentrations, the majority being present in trace amounts. The principal methods for demonstration of heterogeneity and for separation of defined components in a high degree of purity are precipitation by various salts or organic compounds, electrophoresis, ultracentrifugation, ion-exchange chromatography, filtration on gel columns, and immunoprecipitation with antibody-containing antisera. Electrophoresis of serum in free solution or on paper strips enables separation of five major fractions called albumin and α_1-, α_2-, β-, and γ-globulins (**Fig. 3**). Electrophoresis on starch or polyacrylamide gels and agar immunoelectrophoresis reveal the presence of more than 30 different protein components in serum. More than 60 protein components have been identified and characterized.

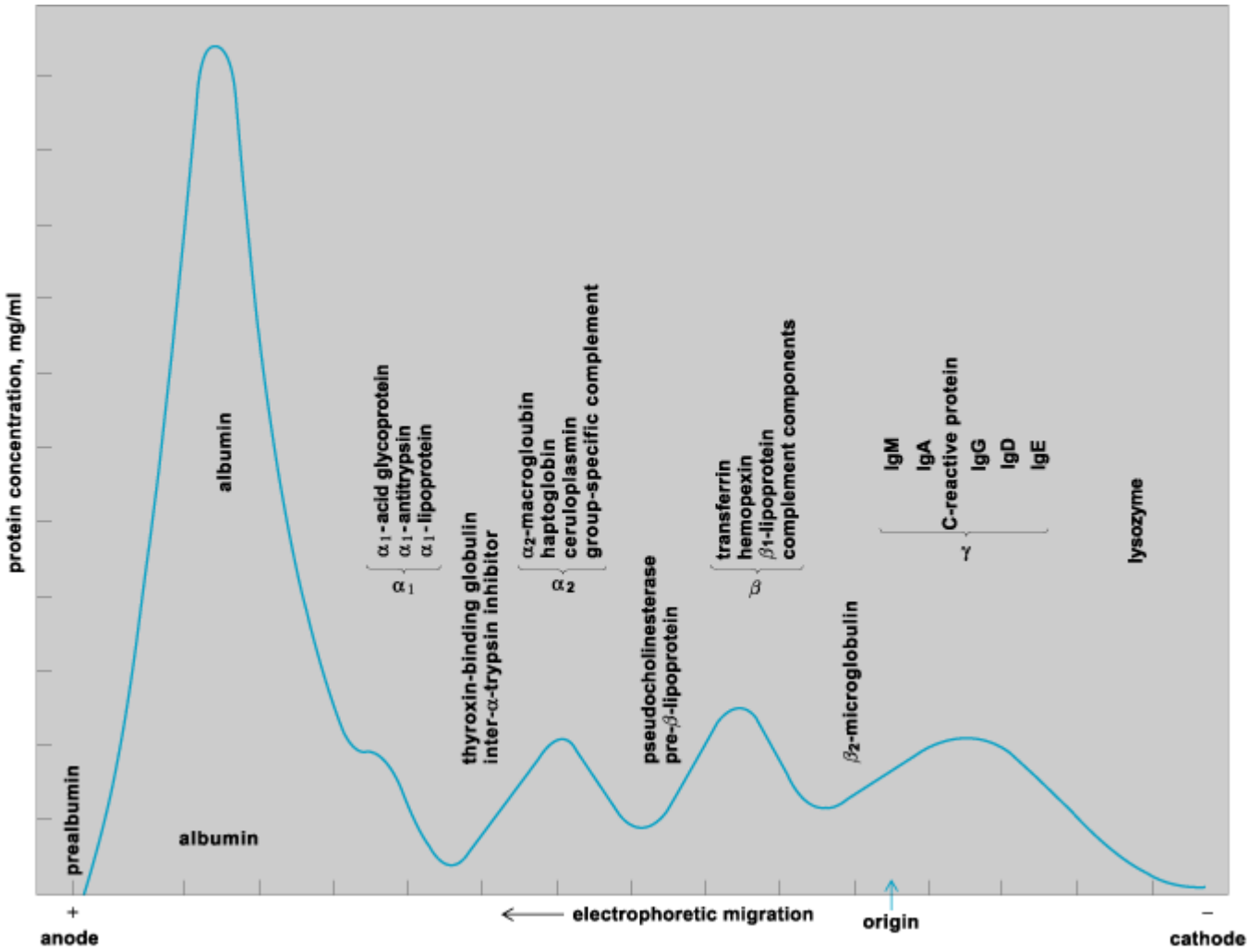

Fig. 3 Paper electrophoresis of normal human serum. Demonstrated is the distribution of several serum proteins in five major electrophoretic fractions, that is, albumin and α_1-, α_2-, β-, and γ-globulins.

Albumin

This protein makes up more than one-half of the total plasma proteins and has a molecular weight of 69,000. Because of its relatively small molecular size and its high concentration, albumin contributes to 75–80% of the colloid osmotic pressure of plasma. It plays, therefore, a major role in the regulation of the intravascular volume and the fluid exchange between the vascular system and the extravascular space. In addition, albumin serves as a transport protein for various substances. It carries small ions, such as calcium and iodine, as well as organic compounds like bilirubin.

Immunoglobulins

The immunoglobulins, which represent approximately one-sixth of the total protein, largely constitute the γ-globulin fraction. The immunoglobulins are antibodies circulating in the blood, and thus are also called humoral antibodies. They are of great importance in the organism's defense against infectious agents, as well as other foreign substances. Of the different classes of immunoglobulins that can be distinguished, the principal ones are IgG, IgM, IgA, IgD, and IgE. The molecular structure, including the amino acid sequence, of several antibodies has been elucidated, at least in part. Antibodies are formed under the stimulus of a foreign substance, the antigen, and are specifically directed against this antigen. The specificity of an antibody reaction appears to be ensured by a specific molecular structure in certain parts of the antibody molecule. In addition, inherited structural variations are recognized in molecular regions not concerned directly with the antigen-antibody reaction. Immunoglobulins are thus a complex mixture of a large number—in the order of 10,000–100,000— structurally

different antibody molecules. Humoral antibodies are present in most vertebrates, apparently lacking only in certain primitive fishes. Comparative analysis of antibody structure in different species becomes increasingly important for the understanding of evolution. *See also:* **Immunoglobulin (/content/immunoglobulin/338600)**

Other proteins

The lipoproteins are another class of serum proteins and make up slightly less than 10% of the total. Presumably they serve as transport proteins for lipids, such as cholesterol, cholesterol esters, and phospholipids. Three major classes can be differentiated: the α_1-, prebeta-, and β_1-lipoproteins.

A number of other serum proteins function as carriers for specific substances. These include transport proteins for metal ions such as the iron-binding protein, transferrin, and the copper-binding protein, ceruloplasmin. The thyroxin-binding globulin transports the thyroid hormone, and transcortin the steroid hormones. Hemoglobin is eliminated from the circulation by haptoglobin, and heme is bound to hemopexin.

Several serum proteins have the capacity to inhibit proteolytic enzymes, thereby protecting serum and possibly tissue proteins against enzymatic degradation. Among others, these include α_1-antitrypsin and the inter-α-trypsin inhibitor. Present in appreciable concentrations are several other glycoproteins, for instance the α_2-macroglobulin and α_1-acid glycoprotein, whose biological functions are not clearly established. A variety of enzymes are also present in plasma, in addition to an array of clotting factors.

Of considerable interest are the complement components. Complement is an important effector system in immune reactions, the target being the cell surface membranes. Its action may result in cell lysis, directed migration of cells, and preparation of damaged cells for uptake and removal by other cells, a process called phagocytosis. *See also:* **Complement (/content/complement/152500)**

On the one hand, the principal sites of synthesis appear to be the liver cells, where albumin, fibrinogen, α_1-acid glycoprotein, and others are synthesized, and on the other hand, the plasma and lymphoid cells, which are the sites of formation of immunoglobulins and several complement components.

Many plasma proteins of humans and other vertebrates are present in different molecular forms in different individuals. These structural variations are genetically determined. Thus, in addition to the well-known blood groups, there also exist inherited serum protein groups. Examples are the haptoglobins, the group-specific components, which are α_2-globulins with the capacity to bind and transport vitamin D, the different genetic groups of immunoglobulins, and variants of the enzyme pseudocholinesterase. *See also:* **Blood groups (/content/blood-groups/087700)**

Apart from these inherited qualitative differences, genetically controlled defects of serum proteins exist, that is, the complete or almost complete absence of one or another protein. Some deficiencies are well tolerated by the affected individuals, as analbuminemia and ahaptoglobinemia, the inherited defects for albumin and haptoglobin, respectively. Other defects, however, lead to severe diseases. Immunoglobulin defects (the most common form is agammaglobulinemia, or the lack of γ-globulin) result in increased susceptibility for bacterial infections. These individuals suffer, if left untreated, from severe and recurrent infections. Another example is the defect of the copper-binding protein ceruloplasmin in Wilson's disease, a grave inherited condition with copper deposition in brain, liver, and kidney.

Many serum proteins show changes in their concentrations during disease states. The determination of serum levels of certain proteins is, therefore, important for diagnostic purposes. The most striking abnormalities are observed in a malignant disorder of the plasma cell system called myeloma and in a disease of the lymphoid cell system known as macro-

globulinemia Waldenström. The former is commonly associated with the presence of large amounts of a homogeneous protein of the IgG, IgA, IgD, or IgE class in the patient's serum. The latter is characterized by the presence of an increased homogeneous IgM (γ-macroglobulin) fraction. Other serum proteins show altered concentrations in diseases connected with inflammations, with tissue destruction, or with increased loss of proteins into the urine due to kidney damage. In many infections the C-reactive protein appears in measurable quantities in serum. Damage of liver cells leads often to impairment of protein synthesis. Subsequently, serum levels of albumin and clotting factors may decrease. This results in disordered fluid regulation with accumulation of extravascular fluid, particularly in the abdomen, and in bleeding tendency. *See also:* **Clinical pathology (/content/clinical-pathology/141100)**

Other constituents

In addition to the proteins, many other important classes of compounds circulate in the blood plasma. Most of these are smaller molecules which diffuse freely through cell membranes and are, therefore, more similarly distributed throughout all the fluids of the body and not as characteristic for plasma or serum as the proteins.

In terms of their concentration and their function, the electrolytes are most important. They are the primary factors in the regulation of the osmotic pressure of plasma, and contribute also to the control of the pH. The chief cations are sodium, potassium, calcium, and magnesium. The chief anions are chloride, bicarbonate, phosphate, sulfate, and organic acids. Sodium and chloride are present in the highest concentrations. Potassium, although present in low concentrations, is of considerable importance, and alterations of potassium metabolism may result in hypo- or hyperpotassemia. These occur in a variety of diseases, in which symptoms involve chiefly the muscles and particularly the heart muscle, with characteristic changes in the electrocardiogram. *See also:* **pH regulation (biology) (/content/ph-regulation-biology/504050)**

The circulating blood, the system which connects the different parts of the body, also contains the many small compounds which are transported to the sites of synthesis of larger molecules in which they are incorporated, or which are shifted as products of metabolic breakdown to the sites of their excretion from the body. Urea, uric acid, creatinine, and pyruvic acid, important organic metabolites of plasma, are significantly increased in kidney diseases and bring on the symptoms of uremia. Glucose is also an important constituent of plasma because it is a major source of energy for cells throughout the body. Nonesterified fatty acids may, in addition, serve as a source of energy. Free amino acids, the constituents of peptides and proteins, circulate in plasma. Furthermore, bilirubin, vitamin A, steroid hormones, and small peptides like angiotensin and bradykinin are among the many substances present in plasma. Many of these compounds are bound to plasma proteins while they are transported in the blood. This complex formation results generally in a reversible, temporary inactivation of the compound that is being circulated.

Hartwig Cleve

Blood Coagulation

When mammalian blood is shed, it congeals rapidly into a gelatinous clot of enmeshed fibrin threads which trap blood cells and serum. Modern theories envision a succession of reactions leading to the formation of insoluble fibrin from a soluble precursor, fibrinogen (factor I). *See also:* **Fibrinogen (/content/fibrinogen/255900)**

Thrombin

The agent ultimately responsible for the formation of fibrin is a proteolytic enzyme, thrombin, which splits four small polypeptide fragments, the fibrinopeptides, from each molecule of fibrinogen. The remainder of the fibrinogen molecule, now called fibrin monomer, polymerizes to form insoluble fibrin, the structure of the clot. The strands of fibrin are given added

strength through covalent bonds between adjacent fibrin monomers, brought about by the action of a second enzyme, the fibrin-stabilizing factor (fibrinase, factor XIII).

Thrombin does not exist as such in circulating blood but is generated during clotting from an inactive precursor, prothrombin (factor II). Under physiologic conditions thrombin is generated through one of two mechanisms, known as the extrinsic and intrinsic pathways. The extrinsic pathway comes into action when blood comes into contact with injured tissues, which provide a protein-phospholipid complex, tissue thromboplastin. The interactions of tissue thromboplastin, calcium ions, and several plasma proteins, including factor VII (formerly called proconvertin or pro-SPCA), Stuart factor (factor X), and proaccelerin (labile factor or factor V), lead to the formation of a prothrombin-converting principle which transforms prothrombin into thrombin.

Other clotting factors

Blood also clots when it touches glass or other negatively charged surfaces, through reactions described as the intrinsic pathway. The steps in the intrinsic pathway are complex and involve the participation of at least eight soluble protein factors, leading to the formation of the prothrombin-converting principle. These factors include, in the apparent order of their participation, Hageman factor (factor XII, the agent affected by glass), Fletcher factor (a plasma prekallikrein), high-molecular-weight kininogen (Fitzgerald factor), PTA (plasma thromboplastin antecedent, factor XI), Christmas factor (plasma thromboplastin component, factor IX), anti-hemophilic factor (factor VIII), Stuart factor, proaccelerin, and prothrombin. Several of the steps in this process are dependent upon the presence in blood of calcium ions and of phospholipids, the latter derived principally from blood platelets.

The coagulation of blood can also be induced by certain snake venoms which either promote the formation of thrombin or clot fibrinogen directly, accounting in part for their toxicity. Bacterial enzymes, such as staphylcoagulase, derived from *Staphylococcus aureus*, may also induce clotting.

Liquid-state maintenance

The liquid state of the blood is maintained in the circulation by inhibitors in the blood itself and by the action of the liver and the reticuloendothelial system. It is also possible that small clots formed inadvertently within blood vessels may be dissolved by the plasma proteolytic enzyme, plasmin. *See also:* **Plasmin (/content/plasmin/526100)**

Platelets

Platelets, besides furnishing phospholipids for the clotting process, help to stanch the flow of blood from injured blood vessels by accumulating at the point of injury, forming a plug. Platelets participate in the phenomenon of clot retraction, in which the blood clot shrinks, expelling liquid serum. Although the function of retraction is unknown, individuals in whom this process is impaired have a bleeding tendency.

Function of clotting process

The principal function of the clotting process is to check the flow of blood from severed vessels. The clotting mechanism is also concerned with the process of thrombosis, that is, the formation of a clot (thrombus) within blood vessels. The earliest step in the intrinsic pathway, the alteration of Hageman factor by contact with glass, is intimately associated with inflammation, initiating chemical processes which lead to the liberation of small polypeptides known as kinins which induce pain, dilate and increase the permeability of small blood vessels, and promote the accumulation of leukocytes. *See also:* **Thrombosis (/content/thrombosis/694600)**

Hereditary defects

Hereditary deficiencies of the function of each of the protein-clotting factors have been described, notably classic hemophilia (in which antihemophilic factor is present in a nonfunctional form) and Christmas disease (the deficiency of Christmas factor), which are disorders of males and clinically indistinguishable. The various hereditary functional deficiencies are associated with a bleeding tendency with the inexplicable exception of Hageman trait, the inherited deficiency of Hageman factor, Fitzgerald trait (the inherited deficiency of high-molecular-weight kininogen), and Fletcher trait, the inherited deficiency of Fletcher factor. Acquired deficiencies of clotting factors, sometimes of great complexity, are also recognized. Therapy for bleeding due to deficiencies of clotting factors often includes the transfusion of blood plasma or fractions of plasma rich in particular substances the individual may lack. *See also:* **Hemophilia (/content/hemophilia/313900)**; **Human genetics (/content/human-genetics/324600)**

Coagulability tests

Clinical tests of the coagulability of the blood include (1) determination of the clotting time, that is, the time elapsing until shed blood clots; (2) the prothrombin time, the time elapsing until plasma clots in the presence of tissue thromboplastin (and therefore a measure of the extrinsic pathway of clotting); (3) the partial thromboplastin time, the time elapsing until plasma clots in the presence of crude phospholipid (and therefore a measure of the intrinsic pathway of clotting); (4) the enumeration of platelets; and (5) crude quantification of clot retraction and of the various plasma protein-clotting factors. The specific diagnosis for deficiency of each of the clotting factors requires an analysis of the characteristics of the person's plasma and, in many cases, direct comparison of such plasma with that of individuals known to be deficient in the factor in question.

Role of vitamin K

Prothrombin, factor VII, Stuart factor, and Christmas factor are synthesized in the parenchymal cells of the liver in the presence of vitamin K, supplied largely by leafy vegetables and intestinal bacteria. Deficiency of vitamin K, or its inhibition by ingested coumarin compounds, impairs the synthesis of the factors and decreases the coagulability of blood. Fibrinogen and proaccelerin are also synthesized in the liver, and antihemophilic factor is synthesized at least partly in endothelial cells, but the site of synthesis of other factors is not known. *See also:* **Vitamin K (/content/vitamin-k/734600)**

Heparin

Heparin, a polysaccharide–sulfuric acid complex found particularly in the liver and lungs, impairs coagulation by interfering with the formation of the prothrombin-converting principle and with the action of thrombin; its presence in normal blood is disputed. Both coumarin and heparin are used clinically to impede coagulation in thrombotic states, including thrombophlebitis and coronary heart disease. *See also:* **Circulation (/content/circulation/137300)**; **Heparin (/content/heparin/314600)**

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